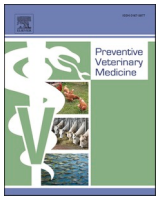
Preventive Veterinary Medicine 210 (2023) 105799

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed



The costs of chronic mastitis: A simulation study of an automatic milking system farm

John Bonestroo [a,b,c,*], Nils Fall [b], Henk Hogeveen [c], Ulf Emanuelson [b], Ilka Christine Klaas [a], Mariska van der Voort [c]

[a] DeLaval International AB, Gustaf De Lavals väg 15, 147 21 Tumba, Sweden
[b] Swedish University of Agricultural Sciences, Dep't Clinical Sciences, POB 7054, SE-750 07 Uppsala, Sweden
[c] Wageningen University and Research, Business Economics Group, Hollandseweg 1, 6706 KN Wageningen, the Netherlands

ARTICLE INFO

Keywords:
Monte Carlo
Simulation model
Mastitis
Chronic
Automated milking system

ABSTRACT

Mastitis is a production disease in dairy farming that causes economic losses. Especially chronic mastitis (i.e., mastitis cases continuing longer than 28 days) can substantially affect the risk of transmission of intramammary infections (**IMI**) and total milk production losses. Insights into the impact of chronic mastitis on production and farm economics are needed to guide chronic mastitis decision-making. We aimed to estimate the costs of chronic mastitis with a Monte Carlo simulation model in which the costs of chronic mastitis were estimated as part of the total mastitis costs. The model simulated milk yields, IMI dynamics, somatic cell count (**SCC**), and pregnancy status on an average Dutch dairy farm with 100 cow places over 9 years. The model was parameterized using information from the literature and actual sensor data from automatic milking system (**AMS**) farms. The daily subclinical milk production losses were modeled using a generalized additive model and sensor data. Transmission of IMI was modeled as well. The model results indicated median total costs of mastitis of € 230 per generic IMI case (i.e., a weighted average of all pathogens). The most substantial cost factors were the extra mastitis cases due to transmission, culling, and milk production losses. Other significant costs originated from dry cow treatments and diverted milk. The model also indicated median total costs due to chronic mastitis of € 118 (51 % of the total mastitis costs). The share of chronic mastitis relative to the total mastitis costs was substantial. Transmission of contagious bacteria had the largest share among the chronic mastitis costs (51 % of the costs of chronic cases). The large share of chronic mastitis costs in the total mastitis costs indicates the economic importance of these mastitis cases. The results of the study point to the need for future research to focus on chronic mastitis and reducing its presence on the AMS dairy farm.

1. Introduction

Mastitis is a common production disease in dairy farming; it can cause compromised animal welfare as well as high economic losses (Hogeveen et al., 2019). Mastitis can be established for a brief period, followed by a quick recovery. However, the mastitis manifestation can also last longer and become chronic. Chronic mastitis is defined as a long-term episode of mastitis (International Dairy Federation, 2011), with somatic cell counts (**SCC**) elevated for at least 3–4 weeks (Bonestroo et al., 2021). A chronic case is less likely to recover if the mastitis case is lengthier in time (Bonestroo et al., 2021). Chronic mastitis cases can substantially affect the number of transmissions of intramammary infections (**IMIs**) (Swinkels et al., 2005a, 2005b; Zadoks et al., 2003) and the total milk production losses (Hadrich et al., 2018).

In automatic milking systems (**AMS**), mastitis detection occurs by continuous sensor monitoring of the milk composition (Hogeveen et al., 2010). Contrary to on-farm sensors, dairy herd improvement associations (**DHI**) utilize milk recordings where milk samples are taken approximately once per month and SCC is measured in a laboratory. Typically, the results from the last two or three monthly measurements are used (St. Rose et al., 2003) to define chronic mastitis with data from the DHI. On-farm AMS SCC sensors allow for much more frequent measurements of SCC. The higher frequency of measurements of on-farm SCC sensors (Nørstebø et al., 2019) can provide a more precise definition of chronic mastitis and consequently a more detailed study of chronic mastitis. Understanding the consequences of chronic mastitis is

* Correspondence to: Hollandseweg 1, Wageningen, the Netherlands.
E-mail address: John.bonestroo@delaval.com (J. Bonestroo).

https://doi.org/10.1016/j.prevetmed.2022.105799
Received 24 March 2022; Received in revised form 9 November 2022; Accepted 12 November 2022
Available online 17 November 2022

essential in developing its management. Therefore, it is vital to gain insights into a major consequence of chronic mastitis, namely the associated costs.

A number of studies have investigated aspects of the cost of chronic mastitis in the past. Steeneveld et al. (2007) showed that antibiotic treatment of chronic mastitis caused by *Streptococcus uberis* was unprofitable, while Swinkels et al. (2005b) showed that a 3-day treatment of chronic mastitis caused by *Streptococcus* spp. was profitable. Both studies emphasized the importance of herd and cow characteristics (e.g., bacterial flora or cow history) in determining the profitability of treating chronic mastitis. However, both studies used monthly DHI SCC measurements to define chronic mastitis. Moreover, these studies did not assess the costs of chronic mastitis at the herd level, but assessed the benefit of treatment of chronic cases on a cow-by-cow basis. To our knowledge, the specific costs of chronic mastitis on the herd level have never been investigated. In the past, herd-based bioeconomic model studies have focused on the overall costs of (subclinical) mastitis (Down et al., 2013; Halasa et al., 2009b) with limited attention paid to the costs of chronic mastitis.

This study, therefore, aimed to estimate the costs of chronic mastitis on an AMS farm. The costs of chronic mastitis were defined as the costs from the start of the chronic episode until its end. These costs were estimated by a Monte Carlo simulation model. The model was parameterized to represent a typical Dutch AMS farm. This model was new and developed for this study, as to our knowledge, no other herd-level bioeconomic simulation models have been applied to estimate chronic mastitis costs.

2. Method

2.1. Model overview

A stochastic Monte Carlo bioeconomic simulation model was developed and used to simulate IMI, general mastitis, and chronic mastitis. The consequences of IMI and mastitis were included in the model, such as milk production losses and clinical mastitis. In a Monte Carlo simulation, an outcome is simulated dependent on variables that have (random) distributional properties. The distributional properties for the variables in our simulation model are given in Table A1 and Table A2 in Appendix A. The model ran a predefined number of times (model iterations), creating different outcomes for every model iteration. The set of outcomes of each model iteration was taken together to form outcome distributions (Dijkhuizen and Morris, 1997; Hogeveen et al., 2019). These outcome distributions were summarized using the 25th, 50^{th,} and 75th percentiles.

The model mimicked a Dutch AMS dairy farm with 100 cow places, with IMIs caused by *Staph. aureus*, *Strep.* spp., Gram-negative bacteria, and non-aureus staphylococci **(NAS)**, and subclinical and clinical mastitis caused by IMIs. The focus of the model was on the estimation of the cost of chronic mastitis; it also covered a range of cow and herd level processes (e.g., culling, milk yield loss, antibiotic treatments) that are associated with chronic mastitis. The cow-places were simulated every day for 9 years for 500 iterations. A burn-in period was set to 2 years and is included in the 9 year simulation. The 2-year burn-in period was based on initial experimentation showing stabilization of ongoing IMI cases occurred at around the 1.5 year mark, and the number of lactating cows in the herd stabilized in 2 years. Standard management was simulated for culling and antibiotic treatment during lactation and dry-off.

The dynamics of IMI in the model were based on literature sources (see Appendix A). These dynamics include clinical mastitis incidence rates, pathogen populations, (contagious) transmissions, and lactational and dry cow period cure rates. Simulation of SCC was based on literature sources in Appendix A and the SCC data used in Bonestroo et al. (2022). Milk yield simulation was based on an adapted statistical model used by Bonestroo et al. (2022) (see Milk yield section). Price data was gathered mostly from secondary databases and recent publications (Appendix A).

The model architecture distinguished between non-transmission IMI cases, which were simulated, and transmission IMI cases, which were modelled outside the simulation. There is a large uncertainty in transmission parameters (i.e., Dalen et al., 2019a or Deng et al., 2021 have a large confidence interval in their estimated transmission rate), and keeping the transmission outside the simulation provided a direct estimate of the economic effect of transmission which did not influence the level of other cost factors. Even if the transmission is overestimated or underestimated, it would not influence the value of the other cost factors, limiting the influence of possible misspecification of transmission. By still having an estimation of the effect of transmission outside the model, we will still able to access the uncertain but possibly large influence of transmission (Dalen et al., 2019a; Deng et al., 2021; Down et al., 2013). Both types of cases are pathogen-specific (e.g. Staph. aureus, gram-negative species, Strep. spp., and CNS). Non-transmission initial cases were cases that are directly simulated by the model; these are simulated using the incidence rate input in the model. Negative consequences (i.e., loss of milk yield, treatments, culling) of non-transmission cases were directly calculated in the model. Differently, the transmission cases were calculated post hoc, after the model has been run, and are defined as cases that are directly transmitted from initial non-transmission cases. These are the clusters of secondary infections that can be calculated after the initial infection in the herd. The cases were determined based on the number of infection days of the non-transmission cases after the current model iteration together with a pathogen-specific transmission rate (see Appendix A). This calculation was performed by taking the infection days of the non-transmission cases (i.e., days with ongoing infection) of different pathogens and multiplying with the pathogen-specific transmission rate, while adjusting for further transmission of transmission cases (see Transmission section). The consequences of transmission cases are captured by multiplying the average pathogen-specific case cost in the model iteration with the total expected pathogen-specific transmission cases. The difference in the model between transmission and non-transmission cases was a useful simplification in comparison to modelling the complete transmission dynamics. The simplified method used, allows the calculation of transmission costs directly. Both types of cases were used to calculate the incidence rate of IMI, the turnover rate, and the incidence rate of clinical mastitis on the farm. The costs of an individual transmission case were considered equal to the average costs of a non-transmission case of the same pathogen in that model iteration.

2.2. Model details

2.2.1. Initial state

An initial state of the cows had to be set prior to running the model, this concerned the days in milk (**DIM**), pregnancy status, and parity. To initiate DIM, we used a discrete uniform distribution from 1 to the day of pregnancy + 270 days. To initiate the parity of cows at the start of the model run, we used a distribution of parities (Poisson with a mean of 1 plus a constant of 1). For the pregnancy status, a DIM at which a cow in the cow place would become pregnant was sampled for every cow place using a DIM pregnancy distribution (e.g., cow place 5 will get pregnant at 70 DIM, see Pregnancy section). The model started on day 1 of the simulation model with no IMIs. We used a burn-in period of two years. This was to stabilize the number of cow places with an active IMI, the number of lactating cows per day in the herd, and remove the effect of the initial set state of the herd on the results.

2.2.2. Pregnancy

To simulate the pregnancy of each cow in a cow place in the model, we used a zero-inflated Poisson distribution (i.e., a Poisson distribution with a specific probability of a 0 value) that modeled the DIM at which a cow in the cow place started to be pregnant. If the current DIM was larger than the DIM of the start of pregnancy, the cow in the cow place was regarded as pregnant. If the DIM of the start of pregnancy for a cow

in a cow place was 0, the cow in the cow place would never become pregnant during the current lactation. Whenever the DIM was equal to 1 for a cow place in the lactation, the start of pregnancy DIM was resampled for the new lactation. The cow would start her dry cow period 210 days after pregnancy start. Pregnancy was used to determine whether the cow occupying the cow place would be culled for fertility problems. The cow in the cow place was culled when the cow in the cow place was not pregnant and the DIM became equal to or larger than 250. Culling made the cow place empty and a cow of parity 1 was to be introduced after a replacement period, which was sampled from a Poisson distribution.

2.2.3. IMI dynamics

To model the onset of a non-transmission IMI episode, we used a probability of IMI occurrence for every DIM for primiparous and multiparous cows (see Appendix B for the method to obtain the probability by using SCC data as a proxy to obtain the distribution of IMI throughout the lactation), similar to Østergaard et al. (2005). Only single IMIs on cow-level (i.e., not having multiple IMIs at the same time) were considered in the simulation model, as there was not enough data or information from the literature available to model the consequences of the interactions of multiple IMIs. The base probability of obtaining an IMI was adjusted when cows had an IMI earlier in the same lactation by a factor of 1.2 (increased probability) (Østergaard et al., 2005). The probability was also adjusted when the cow in the cow place received dry cow treatment at the end of the preceding dry period by a factor of 0.61 (decreased probability during the first 21 days of the new lactation) (Halasa et al., 2009c). If an IMI-free cow in the cow place obtained an IMI, the pathogen was determined by a multinomial distribution based on pathogen share in the IMI pathogen population (i.e., *Staph. aureus*, Gram-negative pathogens, *Strep.* spp., and NAS), adapted from Taponen et al. (2017).

Spontaneous recovery from non-transmission IMI was modeled with a pathogen-specific probability. If the cow in the cow place was determined to have spontaneously recovered from the IMI, the time to recovery was drawn from a pathogen-specific duration distribution (Table A1). If the cow in the cow place did not recover spontaneously, IMI status was set to the specific pathogen for the remainder of the model run. This IMI status could subsequently change due to interventions (further described in the Measures section below).

2.2.4. Pathogen transmission

Transmission in this study is strictly constricted to the transmission of contagious bacteria and therefore it does not consider environmental bacteria. The transmission of pathogens between cows was calculated for the whole herd at the end of each model iteration. The number of infection days during the model iteration of each pathogen was multiplied by a pathogen-specific transmission parameter (β_i expected number of transmission cases per infected day) based on Dalen et al. (2019a) and Skarbye et al. (2021). However, transmission cases could possibly transmit further if $\beta_i * Duration_i$ (transmission parameter tines the median duration of episode of pathogen i) < 1 and we assume that the median duration and transmission parameter remains constant, transmissions would be a converging infinite geometric series (De Serres et al., 2000). Eq. (1) gives the final number of expected transmissions, including all recurrent transmissions of transmissions over an infinite time window. In Eq. (1), the rate of transmission was adjusted for all possible secondary infections. In this case $\frac{1}{1-\beta_i * Duration_i}$ would give the number of infection days per pathogen i per infection day including all recurrent transmissions and the original infection day (De Serres et al., 2000). In Eq. (1), we substracted 1 from $\frac{1}{1-\beta_i * Duration_i}$ to remove the original infection day (which is not from a transmission case). Furthermore, we divided it by the median infection duration to attain the number of expected transmission cases per infection day. These cases were summed, forming the total number of transmission cases (Eq. (1)).

$$N_{transmission} = \sum_{i=1}^{|I|} \sum_{j=1}^{|J|} \sum_{k=731}^{|K|} \frac{\frac{1}{1-\beta_i * Duration_i} - 1}{Duration_i} Case_{i,j,k} \quad (1)$$

where $N_{transmission}$ is the number of transmission cases caused by all pathogens, I = (1,2,3,4) for *Staph. aureus*, Gram-negative pathogens, *Strep*. spp., and NAS ($|I|$ is the size of the set I), $J = (1,\ldots$ Number of cow places) ($|J|$ is the size of the set J), K = (731 days…3285 days) (the simulated days without the burn-in period of 2 years, i.e. starting at day 2 *365 +1 =731 and ending on 9 *365 =3285 days, $|K|$ is the size of the set K), β_i is the transmission parameter for pathogen i, and $Case_{i,j,k}$ is a binary parameter indicating an active IMI in a non-transmission case (1 =True, 0 =False) for pathogen i at cow place j for day k, and $Duration_i$ is the median duration of an IMI of pathogen i.

2.2.5. Clinical mastitis

The occurrence of clinical mastitis for non-transmission cases was based on the IMI status of the cow in the cow place. The model specified two ways an IMI episode could turn into a clinical mastitis episode. Firstly, at the beginning of an IMI episode, the cow had a pathogen-specific probability to turn into a clinical mastitis episode. When it turned clinical, the model drew the duration of the clinical mastitis episode with clinical signs, and simulated it. Secondly, for cows with an IMI but no clinical mastitis signs (subclinical mastitis), the model simulated whether these cows would start a new clinical episode (a flare-up) with a pathogen-specific probability. More specifically, at the start of a new subclinical episode (i.e., at the start of a new IMI episode or when previous clinical signs have subsided), there was a pathogen-specific probability of a flare-up at a later date during the same IMI episode. When there was going to be a future flare-up, each day during the remaining episode had an equal probability of being the day of the flare-up. Whether an episode turned clinical from the start or due to a flare-up, the duration of the clinical episode was sampled from a clinical mastitis duration distribution (Table A1).

The non-transmission IMI incidence rate of primiparous and multiparous cows was calibrated (i.e., tried multiply values) so that the overall clinical mastitis incidence rate for the years after the burn-in was close to 0.28 per cow year (calibration). This value is the median clinical mastitis incidence rate reported in the Netherlands (Santman-Berends et al., 2015). Each clinical mastitis episode was assigned a clinical mastitis severity class (mild, moderate, or severe) according to a pathogen-specific probability distribution (Oliveira et al., 2013; Østergaard et al., 2005).

A conceptual clinical mastitis detection process was implemented. The clinical mastitis detection process was modeled with a sensitivity and a specificity parameter, see Table A1. Specificity was interpreted as a probability of a true negative for a random healthy cow in a cow place, and where $1 - \text{specificity}$ was the probability of a false positive. Sensitivity was interpreted as a probability of a true positive for a random sick cow in a cow place. It was determined whether clinical mastitis was detected for every day and cow place. If the cow in a cow place had clinical mastitis, the probability that the clinical mastitis was detected was equal to the sensitivity parameter. If the cow in the cow place had no clinical mastitis, the probability that the clinical mastitis detection process showed that the cow in the cow place had clinical mastitis was equal to $1 - \text{specificity}$.

2.2.6. Somatic cell count

The SCC for non-transmission cases was simulated at the start of an IMI episode and depended on if the cow in the cow place would recover from the IMI episode. The recovery process is described in the IMI dynamics and Measures section. The IMI recovery process is explained in IMI dynamics. The SCC for recovered and non-recovered cases was handled separately.

At the start of recovering cases, SCC data points were sampled from

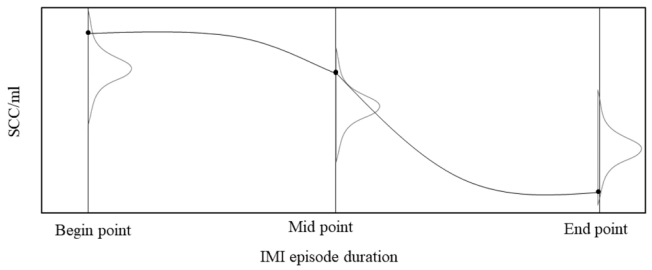


Fig. 1. The process of sampling SCC measurements (the dots) at the start point, mid point, and end point and interpolating the points in between the dots (the line) during a recovering IMI episode (points and line are only an example). The distributions in the figure indicate the distributions that are used to sample SCC at the begin, mid, and end point of a recovering SCC episode.

the pathogen-specific SCC distributions for the start point (day 1 of the episode), mid point (day halfway of the episode), and end point of the IMI episode (the last day of the episode). Next, the data points between the starting, mid, and end point were interpolated using a cubic spline (i.e., a nonlinear piecewise third-order polynomial) (Fig. 1). An SCC variation distribution was added to the cubic-spline-interpolated SCC values to simulate the day-to-day variation in SCC. This SCC variation distribution was fitted using data used in Bonestroo et al. (2022). It was parameterized as a normal distribution using the difference between an individual SCC sample and the 7-day rolling average of SCC during lactation, resulting in a Normal(0,0.8) distribution. The distribution estimated was similar to the variation distribution used in Østergaard et al. (2005). For the non-recovered cases, SCC samples were equal to a pathogen-specific constant of SCC for non-recovering cases. These samples were combined with samples of the distribution that mimic day-to-day variation used for the recovered cases using addition (SCC *values* + day variation in *SCC*).

For non-IMI SCC measurements, a similar approach was taken as in Østergaard et al. (2005). Using the dataset from Bonestroo et al. (2022), an SCC lactation curve was estimated in a Generalized Additive Model (**GAM**) using SCC (dependent variable) and DIM (independent variable) with a random effect on cow lactation level. The fitted values for 1–305 DIM were obtained and used in the simulation to reflect that SCC tends to be higher in early lactation (Østergaard et al., 2005). If the lactation was longer than 305 DIM, the SCC level was set to the SCC level at 305 DIM. When the SCC at the end of an IMI episode would be higher than the SCC of a healthy cow with the same DIM, the highest SCC was used for the remainder of the cow's life. Additional variation from samples of the SCC variation distribution was added to these non-IMI samples. These final values were used as the non-IMI SCC measurements in the model.

2.2.7. Milk yield

To simulate milk yield and milk yield losses due to mastitis for non-transmission cases, we used DIM, SCC, parity status, and SCC history to estimate the daily milk synthesis rate (kg/hour). This simulation was performed using the GAM proposed in Bonestroo et al. (2022). A GAM is an extension of a general linear model where a dependent variable depends on a combination of non-linear smoothing functions and traditional regression coefficients. GAMs increase the flexibility of general linear model in terms of non-linear associations. These non-linear smoothing function can take any functional form (linear, quadratic, cyclic, or a combination of them) based on the data and with no prior specification of the functional form. As such, milk synthesis rate (milk yield per hour) was estimated using a non-linear smoothing function of SCC for each parity level (1st, 2nd, and 3rd or more parity) and a random effect on cow lactation level. The adapted model differed from the published model by using the SCC history variable rather than the chronicity group variable. The SCC history variable was defined as the number of days with SCC higher or equal to 200,000 SCC/ml divided by 7 days in the lactation up to the current day. It was included to reflect the additive nature of the effect of chronic mastitis on the milk yield (Hadrich et al., 2018). Milk production losses due to subclinical mastitis were calculated by taking the effect of SCC and SCC history on milk synthesis rate from the milk yield GAM (Bonestroo et al., 2022) each day. The milk production rate and losses per hour were multiplied by 24 h to obtain the daily milk yield. This daily milk yield was combined with the treatment status and clinical mastitis milk loss to determine diverted milk for clinical mastitis cases. In the model, it would work as follows: the model simulates a specific second parity cow at 126 DIM with 675.000 SCC/ml and with 7 weeks of SCC > 200,000 during the current lactation. Parity, DIM, current SCC, and weeks with SCC> 200,000 are put into the GAM model, resulting in a milk synthesis rate of 1.23625 kg/hour. This is multiplied by 24 h to obtain a daily yield of 29.67 kg. Furthermore, the partial effects of current SCC and SCC history in the GAM model can be summed and multiplied by 24 h to obtain the subclinical mastitis milk losses.

The base clinical mastitis milk production losses (without the discarded milk due to antibiotic treatment as it is a separate cost factor) were a percentage of milk production over the remainder of the lactation. This parameter was set to 5 % (Hortet and Seegers, 1998; Seegers et al., 2003). This base reduction of daily milk yield was adjusted for clinical mastitis severity using severity class multipliers, adapted from Oliveira et al. (2013). These multipliers ensured that milk production losses due to mild clinical mastitis were lower than those of severe clinical mastitis. Apart from clinical mastitis milk production losses during the same lactation, milk yield losses incurred by clinical mastitis in any current or the previous lactations were estimated to be 3.3 %, adapted from the results of Bar et al. (2007). This is modelled by multiplying the milk yield with 3.3 % for cows that had a clinical mastitis. Milk yield is inverse linked with SCC in the model. As such, the recovery of SCC (i.e., the decrease in SCC) would result in a recovery of milk yield (i.e., an increase in milk yield).

2.2.8. Measures

Standard mastitis measures or interventions were simulated based on pre-set generic decision rules grounded on SCC, DIM, and clinical mastitis data. Each measure also had a pre-specified outcome (stochastic in the case of in-lactation or dry cow treatment) on the state of the cow. The decision rules were initiated for every day in the model:

- Clinical mastitis which is detected but was not treated with antibiotics during the last 20 days: treatment with antibiotics
- Rolling 90-day median SCC higher than 200,000 SCC/ml and not pregnant: cull
- Last day of lactation and having an SCC higher than 150,000 SCC/ml: dry cow treatment

All other combinations of SCC, DIM, and clinical mastitis resulted in no mastitis-related actions. A treatment during lactation had a pathogen-specific probability of resulting in recovery from IMI. If the cow in the cow place was simulated to recover after lactational treatment, the duration of the IMI episode was simulated. Otherwise, the IMI status remained the same.

In the Netherlands, standard practice is to initiate dry cow treatment based on the last known SCC without bacteriological testing (KNMvD, 2018). As such, we modeled the initiation of dry cow treatment based on an SCC cut-off. A current IMI, on the last day of lactation, had a pathogen-specific probability of recovering after dry cow treatment. If the cow in the cow place did not have an IMI, the treatment was still performed. If a cow did have an IMI but was not treated in the dry period, the cow would have a pathogen-specific probability of spontaneously recovering during the dry cow period (see Appendix A). If the cow in the cow place recovered, the IMI status was reset at the beginning of the next lactation.

Lastly, the probability of mortality or culling for non-mastitis-or-

fertility reasons was modeled for each simulation day for all cows (including healthy cows). This possibility was modeled as a constant probability for each cow place and simulation day. Culling is a complex process as such, we applied a simplification to the culling process. This cow culled due to other reasons was treated as a culled case without mastitis-related costs. This process of culling due to other reasons was modelled as a constant probability of dying adapted from the share of cullings due to other reasons as indicated by Bascom and Young (1998) and the mean culling rate in Nor et al. (2014). When a cow was culled, all future mastitis costs concerning that cow would stop.

2.3. Calculation of incidence and turnover rates

Economic outcomes are divided by the number of IMI cases to express outcomes per case of IMI. However, the IMI and clinical mastitis incidence rate were expressed per cow years at risk, while the turnover rate was expressed as per cow year (Eqs. (2)–(4)). In Eq. (3), we assumed that the transmission cases had the same proportion of clinical mastitis as the non-transmission cases. We need to calculate the number of clinical mastitis cases caused by the transmission cases. Therefore, to estimate these cases for transmission cases, the fraction of transmission cases relative to the non-transmission cases is multiplied by the non-transmission clinical mastitis cases. This multiplication would approximate the number of clinical mastitis cases for the transmission cases. Dividing the non-transmission and transmission clinical mastitis cases by the number of cow years at risk would give the clinical mastitis incidence rate per cow year. Cow years at risk are defined as the total number of IMI-free days divided by 365 days. The overall turnover rate was calculated similarly (Eq. (4)).

$$Incidence_{IMI} = \frac{IMI\ Cases_{nt} + IMI\ Cases_{transmission}}{Number\ of\ cow\ years\ at\ risk_{IMI}} \tag{2}$$

$$Incidence_{CM} = \frac{CM\ Cases_{nt} + CM\ Cases_{nt}\left(\frac{IMI\ Cases_{transmission}}{IMI\ Cases_{nt}}\right)}{Number\ of\ cow\ years\ at\ risk_{CM}} \tag{3}$$

$$Turnover\ rate_{All} = \frac{Total\ cullings_{nt} + Mast.cullings_{nt}\left(\frac{IMI\ Cases_{transmission}}{IMI\ Cases_{nt}}\right)}{Number\ of\ cow\ years\ at\ risk_{culling}} \tag{4}$$

where $Incidence_{IMI}$ is the IMI incidence rate per cow year, $IMICases_{nt}$ is the number of the non-transmission IMI cases, $IMICases_{transmission}$ is the number of the transmission IMI cases that were expected based on the non-transmission IMI cases (see Pathogen transmission section),$Incidence_{CM}$ is the clinical mastitis incidence rate per cow year, $CM\ Cases_{nt}$ is the number of non-transmission clinical mastitis cases, $Turnover\ rate_{All}$ is the overall turnover rate that includes non-transmission and transmission cases, $Total\ cullings_{nt}$ is the number of non-transmission cullings due to all reasons (including mastitis), and $Mast.cullings_{nt}$ is the number of non-transmission cullings due to mastitis.

2.4. Economic calculations

In the economic calculations, we estimated the costs of mastitis as the net effect on farm profit based on the non-economic outcomes. These mastitis costs included the costs of milk production losses, treatment, culling, labor, and contagious transmission. Eqs. (5)–(15) give the calculations for the economic outcomes. All outcomes and costs were calculated per pathogen (i) for all cow places (j) and all days (k) and summed up across all pathogens to form the total costs of mastitis. More specifically, I = (1,2,3,4,5) for *Staph. aureus*, Gram-negative pathogens, *Strep.* spp., NAS, and no pathogen respectively, J = (1,… Number of cow places), and K = (731 days,…3285 days).

On the costs of different factors, $Cost_{milk\ loss\ SCM}$ are the costs of subclinical mastitis milk production losses, $Cost_{milk\ loss\ CM}$ are the costs of clinical mastitis milk production losses, $Cost_{milk\ diversion}$ are the costs of milk diversion, $Cost_{treatment}$are the costs of lactational antibiotic treatment due to mastitis, $Cost_{diagnostics}$ are the costs of laboratory analysis to find underlying IMI, $Cost_{DCT}$ are the costs of applying dry cow treatment, $Cost_{labor\ checks}$ are the labor costs of checking clinical mastitis alerts, $Cost_{culling}$ are the costs of culling, $N_{IMI\ cases}$ is the total number of non-transmission cases, and $N_{transmission}$ is the total number of transmission cases. $Cost_{transmission}$ are the total costs of contagious transmission. All costs were also expressed as the pathogen-specific share of the overall chronic mastitis costs.

For the costs of diagnostics, it was assumed that 15 % of the lactational treatments are carried out in combination with bacteriology (diagnostic proportion), adapted from Griffioen et al. (2016). For the costs of lactational treatment, it was assumed that 5 % of the treatments required a veterinarian (proportion veterinary treatment) (Lam et al., 2013).

$$Cost_{milk\ loss\ SCM,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} subclinical\ milk\ loss_{i,j,k} * (milk\ price - feed\ correction) \tag{5}$$

$$Cost_{milk\ loss\ CM,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} clinical\ milk\ loss_{i,j,k} * (milk\ price - feed\ correction) \tag{6}$$

$$Cost_{diagnostics,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} Lactational\ treatment_{i,j,k} * diagnostic\ price * diagnostic\ proportion \tag{7}$$

$$Cost_{diverted\ milk,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} Diverted\ milk_{i,j,k} * (milk\ price - feed\ correction) \tag{8}$$

$$Cost_{lactational\ treatment,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} Lactational\ treatment_{i,j,k} * (lactational\ treatment\ price + labor\ lactational\ treatment * labor\ wage * (1 - proportion\ involvement\ veterinarian) + labor\ lactational\ treatment * veterinarian\ wage * proportion\ involvement\ veterinarian) \tag{9}$$

$$Cost_{labor\ checks,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} Lactational\ treatment_{i,j,k} * labor\ farmer\ check * labor\ wage \tag{10}$$

Table 1
Economic results of the simulation model for the total mastitis costs, and pathogen-specific shares of the total cost (in €) per non-transmission IMI case.

Costs	1st Qu.	Median	3rd Qu.
Total clinical mastitis milk production losses	26.65	29.64	32.93
Total subclinical mastitis milk production losses	22.80	23.81	25.05
Total mastitis culling	21.88	24.55	27.62
Total lactational antibiotics	11.42	12.35	13.15
Total dry cow treatment	11.18	11.73	12.30
Total diagnostic	0.38	0.41	0.43
Total diverted milk	9.23	10.03	10.75
Total clinical mastitis checks	0.39	0.42	0.44
Total extra costs due to transmission	103.48	117.62	133.48
Total mastitis costs	214.94	230.30	249.86
Pathogen-specific share of the total costs			
Total Staph. aureus share	102.76	116.96	135.54
Total Gram-negative pathogens share	8.67	11.01	13.07
Total Strep. spp. share	28.32	32.74	36.92
Total Non-Aureus Staph. share	58.40	66.22	75.77
Total non-pathogen-related share[a]	1.65	1.96	2.33

[a] Costs due to culling cows with high SCC with no pathogen or treating cows with no pathogen.

Table 2
Economic results of the simulation model for the chronic mastitis costs, and pathogen-specific shares of the chronic cost (in €) per non-transmission IMI case.

Costs	1st Qu.	Median	3rd Qu.
Total chronic mastitis milk production loss due to clinical mastitis	5.84	6.72	7.44
Total subclinical mastitis during ongoing non-spontaneously cured IMI milk production losses	10.16	10.96	11.85
Total chronic mastitis treatment	5.50	6.26	6.92
Total chronic mastitis diagnostic	0.18	0.21	0.23
Total chronic mastitis extra costs due to transmission	51.31	59.71	70.85
Total chronic mastitis diverted milk	4.49	5.06	5.70
Total chronic mastitis culling	21.88	24.55	27.62
Total chronic dry cow treatment	3.55	3.90	4.28
Total chronic mastitis costs	106.25	118.10	132.30
Pathogen-specific share of costs			
Total chronic *Staph. aureus* share	71.96	82.85	97.05
Total chronic Gram-negative pathogens share	3.35	5.11	6.82
Total chronic *Strep.* spp. share	11.55	14.41	17.38
Total chronic Non-Aureus Staph. share	12.25	14.36	16.74

$$Cost_{DCT,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} Dry\ cow\ treatment_{i,j,k} * (dry\ cow\ treatment\ price + labor\ dry\ cow\ treatment * labor\ wage) \quad (11)$$

$$Cost_{culling,i} = \sum_{j=1}^{|J|}\sum_{k=731}^{|K|} culled\ due\ to\ mastitis_{i,j,k} * culling\ cost \quad (12)$$

$$Cost_{mastitis\ without\ transmission,i} = Cost_{milk\ loss\ SCM,i} + Cost_{milk\ loss\ CM,i} + Cost_{diverted\ milk,i} + Cost_{lactational\ treatment,i} + Cost_{diagnostics,i} + Cost_{DCT,i} + Cost_{labour\ checks,\ i} + + Cost_{culling,i} \quad (13)$$

$$Cost_{transmission} = \sum_{i=1}^{|I|} \frac{Cost_{mastitis\ without\ transmission,i}}{N_{IMI\ cases,i}} * N_{transmission,i} \quad (14)$$

$$Cost_{mastitis} = Cost_{transmission} + \sum_{i=1}^{|I|} Cost_{mastitis\ without\ transmission,i} \quad (15)$$

2.4.1. Calculation of costs of chronicity

In this study, we specifically investigated the costs due to chronic mastitis. Therefore, the simulation model output associated with chronic cases was used. Days of ongoing chronic cases were identified by an IMI duration of more than 28 days combined with a 28-day SCC mean of more than 200,000 SCC/ml (Bonestroo et al., 2021). When identified as a chronic case, the initial stage (i.e., the 27 days up to the identification) was also designated as chronic. The milk production losses due to subclinical and clinical mastitis, diverted milk, diagnostics, contagious transmission, culling, and the number of treatments on these days were also identified as consequences of chronic mastitis.

Special attention needed to be paid to identifying the transmission of chronic mastitis cases in the model. Eq. (1) was adapted to ensure that only the transmission of more prolonged cases (4 weeks or longer IMI and high SCC) was included in the calculation of the chronic mastitis costs by replacing $Case_{i,j,k}$ with $Chronic_{i,j,k}$ variable (Eq. (16)).

$$N_{transmission\ chronic} = \sum_{i=1}^{|I|}\sum_{j=1}^{|J|}\sum_{k=730}^{|K|} \frac{\frac{1}{1-\beta_i * Duration_i} - 1}{Duration_i} Chronic_{i,j,k} \quad (16)$$

where $N_{transmission\ chronic}$ is the number of transmission cases caused by all IMIs during chronic IMI episodes, I = (1,2,3,4) for *Staph. aureus*, Gram-negative pathogens, *Strep.* spp., and NAS, respectively, J = (1,… Number of cow places), K = (731days,…3285 days), β_i is the transmission parameter for IMI i, and $Chronic_{i,j,k}$ is a binary parameter indicating whether the active IMI is chronic (current episode active for more than 4 weeks, 1 =True, 0 =False) for IMI i at cow place j for day k.

The costs during a chronic mastitis episode were indicated as chronic costs. As such, Eq. (5) until 11 were adapted for chronic mastitis (as in Eq. (16)). and these costs would include: the costs of subclinical and clinical milk production losses, diverted milk costs, the lactational treatment costs, the labor costs of checking clinical mastitis alerts, dry cow treatment costs, and the diagnostic costs. Culling costs due to chronic mastitis were set equal to the culling cost due to mastitis (Eq. (12)) as the farmer would only cull the animals that have a high SCC for 90 days given the current measures. The number of transmissions during chronic episodes was multiplied by the average costs of a mastitis case caused by each pathogen to obtain the costs due to extra transmissions (similar to Eq. (14)). All previously mentioned chronic mastitis costs were summed up to obtain the total chronic mastitis costs. All outcomes and costs were calculated per pathogen as well and expressed as the pathogen-specific share of the overall chronic mastitis costs.

2.4.2. Validation and sensitivity analysis

In this paper, we aimed to simulate the current cost of chronic mastitis and therefore did not alter the decision rules to experiment with them. The model was validated using multiple validation strategies as proposed by Sargent (2010). Firstly, the model was validated using extreme condition tests. We used extreme scenarios to determine whether the model resulted in expected behavior (e.g., setting IMI

Table 3
The median (25 % and 75 % quartiles) economic results of the sensitivity analysis of increasing (+20 %) and decreasing (−20 %) the transmission rate for all pathogens, the lactational cure rate after treatment for all pathogens, and the dry cow treatment cure rate for all pathogens.

	Transmission parameters- 20 %	Transmission parameters + 20 %
Total mastitis costs per case (in €)	196.04 (183.91–208.90)	284.80 (258.08–2310.26)
Total costs due to chronic mastitis per case (in €)	99.37 (90.73–108.89)	147.76 (129.73–166.54)
	Lactational cure rate parameters –20 %	Lactational cure rate parameters + 20 %
Total mastitis costs per case (in €)	273.90 (252.99–300.65)	206.49 (191.40–221.74)
Total costs due to chronic mastitis per case (in €)	141.61 (129.05–158.81)	101.33 (89.22–110.84)
	Dry cow treatment cure rate parameters –20 %	Dry cow treatment cure rate parameters + 20 %
Total mastitis costs per case (in €)	271.88 (250.27–296.37)	201.80 (189.45–216.36)
Total costs due to chronic mastitis per case (in €)	143.00 (129.13–160.28)	99.08(90.49–109.31)

If the resulting lactational or dry cow treatment cure rate was above 100 %, it was capped at 100 %.

incidence rate or transmission to 0 and estimating no mastitis or transmission-related costs). Secondly, traces were used as individual cow places were monitored throughout the simulation to determine consistency, similar to Gussmann et al. (2018). Thirdly, external validation was performed. To assess whether the model reflected the average Dutch dairy farm, we compared the culling or turnover rate of the model with the Dutch average for dairy farms. The turnover rate was in line with the reported Dutch average turnover rate (0.3 cullings per cow year) (Nor et al., 2014).

Lastly, a sensitivity analysis was performed by changing lactational cure rates after treatment for all pathogens, dry cow treatment cure rates for all pathogens, and the transmission parameters for all pathogens, decreasing and increasing them by 20 %. The sensitivity analysis parameters were chosen as they were expected to have the most considerable effects on mastitis costs.

3. Results

3.1. Mastitis dynamics

The model results indicated a median turnover rate of 0.31 with a quartile range of 0.30–0.33 per cow year. The median clinical mastitis incidence rate was 0.27 with a quartile range of 0.24–0.30 cases per cow year. The median incidence rate of IMI was 1.00 with a quartile range of 0.93–1.08 cases per cow year.

3.2. Economics

3.2.1. Total costs of mastitis

Table 1 gives the economic outcomes of the model per IMI case. The median total mastitis costs were € 230 with a quartile range of € 215 to € 250 per IMI case. Most of the costs occurred due to transmission (i.e., transmission cases), culling, and clinical and subclinical milk production losses. Other substantial costs originated from dry cow treatments, lactational treatments, and diverted milk. We could determine that *Staph. aureus* caused the largest share of the total costs of IMI by looking at pathogen-specific economic impact per generic IMI case, followed by NAS, *Strep.* spp., and Gram-negative pathogens.

3.2.2. Costs of chronic mastitis

In Table 2, we present chronic mastitis costs per IMI case and its cost factors. The median total costs due to chronic mastitis were € 118 (51 % of the total mastitis costs) with a quartile range of € 106 to € 132 per IMI case. The share of chronic mastitis relative to the total mastitis costs was substantial. Unsurprisingly, the costs due to transmission had a large share in the chronic mastitis costs (on average 52 % of the total chronic mastitis costs). Culling and milk production losses markedly affected the costs of chronic mastitis as well (on average culling: 21 %, combining subclinical and clinical milk production losses: 15 %). Subclinical mastitis production losses were higher than clinical mastitis production losses compared to the share in the total costs of mastitis. On average, *Staph. aureus* had the largest share in the costs of chronic mastitis (71 %), followed by *Strep.* spp. (12 %), NAS (12 %), and Gram-negative pathogens (4 %). The high share of, *Staph. aureus* can be explained by the low cure rate and a moderate share in the pathogen population, while the other pathogens tend to be less prevalent or have a substantially higher cure rate.

3.3. Sensitivity analysis

In the sensitivity analysis, we assessed the effects of decreasing and increasing the transmission rate of all pathogens by 20 %, lactational cure rates for all pathogens by 20 %, and dry cow treatment cure rates for all pathogens by 20 %. The median (25 % and 75 % quartiles) of total mastitis costs and the chronic mastitis costs are reported in Table 3. The results show that changing the transmission parameters had the most influence on the total and chronic mastitis costs., followed by lactational cure and dry cow cure parameters. We can see that all changes have non-linear effects as a 20 % increase or decrease affect the costs non-proportionally For instance, we can see that reducing transmission rate by 20 % reduces the total mastitis cost by 15 %, while increasing the transmission rate parameters by 20 % increases the total mastitis cost by 24 %.

4. Discussion

This study is not the first study on mastitis costs, but it contains unique features adding to our knowledge of the economic impact of mastitis. Simulation modeling has been frequently used to assess mastitis costs in the past (Hogeveen et al., 2019), but it did not distinguish between non-chronic and chronic mastitis. This study is the first that used a simulation model that estimates the costs of chronic mastitis on a herd basis. Another unique feature of the model was its use of GAM models to model daily milk yields and SCC levels in detail based on real-life milking data. The effect of subclinical mastitis on milk yield was estimated by associating SCC with milk yield in the GAM model. The model results show that chronic mastitis caused a large share of the total costs of mastitis. The chronic mastitis costs mainly were caused by *Staph. aureus* due to its low cure rate.

This study's median total costs of mastitis of € 230 per IMI can be compared to other simulation model studies focusing on Dutch dairy farms. Other studies have calculated the costs of clinical and subclinical cases separately. Huijps et al. (2008) estimated the total costs of € 210 per clinical case and € 53 to € 72 for a subclinical case for an average Dutch dairy farm. Van Soest et al. (2016) estimated a total cost of € 301 per clinical case for an average Dutch dairy farm. Without the transmission cost factor, we would estimate the total costs of mastitis per case to be € 114 per IMI case, based on a combination of clinical and subclinical cases. The estimated costs of IMI in this study were between the costs of clinical and subclinical cases in the other studies. Therefore, the estimated total cost of mastitis was in line with previous results.

The total costs of (chronic) mastitis could be attributed to different cost factors. As such, it was possible to estimate the most crucial factors in mastitis costs. The transmission was found to be an important factor, and others have found comparable results (Down et al., 2013; Gussmann

Table A1
The model parameters in the simulation model with their distribution or value and their sources.

Model parameter	Distribution or value	Reference
Incidence rate non-transmission cases of IMI for primiparous cows	0.28 per cow year	Calibrated to obtain a model-reported incidence rate close to reported in Santman-Berends et al. (2015)
Incidence rate non-transmission cases of IMI for multiparous cows	0.504 per cow year	Calibrated to obtain a model-reported incidence rate close to reported in Santman-Berends et al. (2015)
Culling due to other reasons than fertility or mastitis over each day during lactation as well as during the dry cow period	Uniform(1, $1.145^{1/365}$-1)	Adapted from Nor et al. (2014) and Bascom and Young (1998)
Day in milk at the initiation of the model for cow	Uniform(min = 1, max = 365) where 306–365 is in the dry cow period	Initial initialization
Parity at the initiation of the model for cow	Poison(mean = 1) + 1	Initial initialization
Day in milk of pregnancy distribution	Zero-inflated Negative Binominal distribution (mean = 123.72, sigma = 0.28, probability = 0.05)	Based on a dataset used in Bonestroo et al. (2022) with the addition of pregnancy information. The mean DIM of pregnancy is similar to Berends et al. (2008).
Event IMI	Bernoulli (probability = *a* DIM-specific probability)	Adapted from a DIM-specific probability based on first occurrence of high SCC in dataset used in Bonestroo et al. (2022) multiplied by the incidence rate (Appendix), similar to Østergaard et al. (2005)
Specific IMI occurrence given IMI occurrence	Multinomial(P.aureus = 0.29, P.g.negative = 0.05, P.strep = 0.17, P.NAS = 0.49)	Adapted from Taponen et al. (2017)
Lactational IMI self-recovery *Staph. aureus*	Bernoulli(probability = 0.19)	Van den Borne et al. (2010)
Lactational IMI self-recovery Gram negative	Bernoulli(probability = 0.51)	Fuenzalida and Ruegg (2019)
Lactational IMI self-recovery *Strep.* spp.	Bernoulli(probability = 0.66)	Wilson et al. (1999)
Lactational IMI self-recovery NAS	Bernoulli(probability = 0.46)	Taponen et al. (2006)
Lactational treatment IMI recovery *Staph. aureus* given no self-recovery	Bernoulli(probability = 0.52–0.19)	Sol et al. (2000) and Van den Borne et al. (2010)
Lactational treatment IMI recovery Gram negative given no self-recovery	Bernoulli(probability = 0.70–0.51)	Fuenzalida and Ruegg (2019)
Lactational treatment IMI recovery *Strep.* spp. given no self-recovery	Bernoulli(probability = 0.83–0.66)	Wilson et al. (1999)
Lactational treatment IMI recovery NAS given no self-recovery	Bernoulli(probability = 0.86–0.46)	Taponen et al. (2006)
Duration *Staph. aureus* IMI if cured	Poison(mean = 30)	Sol et al. (2000)
Duration Gram negative IMI if cured	Poison(mean = 18)	Based on the median in survival graph in Fuenzalida and Ruegg (2019)
Duration *Strep.* spp. IMI if cured	Poison(mean = 37.5)	Average of both groups in Zadoks et al. (2003)
Duration NAS IMI if cured	Poison(mean = 28)	Adapted from Bonestroo et al. (2021) with the assumption that most infections were due to NAS and Valckenier et al. (2021) by combining transient and persistent IMI classes for all NAS (assuming that transient IMI can take 14 days)
Clinical mastitis given underlying *Staph. aureus* at first day IMI	Bernoulli(probability = 0.17)	Swinkels et al. (2005a)
Clinical mastitis given underlying Gram negative at first day IMI	Bernoulli(probability = 0.85)	Hogan and Smith (2003)
Clinical mastitis given underlying *Strep.* spp. at first day IMI	Bernoulli(probability = 0.3)	Swinkels et al. (2005b)
Clinical mastitis given underlying NAS at first day IMI	Bernoulli(probability = 0.08)	Todhunter et al. (1993)
Flare-up during the same IMI episode of *Staph. aureus*	Bernoulli(probability = 0.27)	Adapted from Wente et al. (2020)
Flare-up during the same IMI episode of Gram negative	Bernoulli(probability = 0.10)	Adapted from Wente et al. (2020)
Flare-up during the same IMI episode of *Strep.* spp.	Bernoulli(probability = 0.19)	Adapted from Wente et al. (2020)
Flare-up during the same IMI episode of NAS	Bernoulli(probability = 0.02)	Adapted from Wente et al. (2020)
Clinical mastitis episode duration	Poison(mean = 6.11)	Nash et al. (2002)
Clinical mastitis severity class, given *Staph. aureus*	Multinomial(Mild = 0.53 Moderate = 0.47 Severe = 0.00)	Oliveira et al. (2013)
Clinical mastitis severity class, given Gram negative	Multinomial(Mild = 0.32 Moderate = 0.35 Severe = 0.33)	Adapted from Oliveira et al. (2013) by averaging all gram-negative pathogens
Clinical mastitis severity class, given *Strep.* spp.	Multinomial(Mild = 0.61 Moderate = 0.38 Severe = 0.01)	Oliveira et al. (2013)
Clinical mastitis severity class, given NAS	Multinomial(Mild = 0.61 Moderate = 0.37 Severe = 0.02)	Oliveira et al. (2013)
	5 %	Seegers et al. (2003)

(*continued on next page*)

Table A1 (*continued*)

Model parameter	Distribution or value	Reference
Base clinical mastitis milk production losses remainder lactation		
Clinical mastitis milk production losses remainder lactation mild multiplier	-3.7/− 5.1 = 0.725	Oliveira et al. (2013) assuming the differences between mild and moderate hold for the remainder of the lactation
Clinical mastitis milk production losses remainder lactation moderate multiplier	-5.1/− 5.1 = 1	Oliveira et al. (2013)
Clinical mastitis milk production losses remainder lactation severe multiplier	-11.2/− 5.1 = 2.196	Oliveira et al. (2013) assuming the differences between severe and moderate hold for the remainder of the lactation
SCC at the beginning of a *Staph. aureus* IMI episode	Triangular(a = ln(281), b = ln(430), c= ln(355))	Adapted from Dalen et al. (2019a) where the minimum and maximum are based on the 95 % confidence interval
SCC at the mid point of a *Staph. aureus* IMI episode	Triangular(a = ln(100), b = ln(200), c= ln(150))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC at the end point of a *Staph. aureus* IMI episode	Triangular(a = ln(50), b = ln(150), c= ln(100))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC at the beginning of a Gram-negative IMI episode	Triangular(a = ln(1600), b = ln (2500), c= ln(2000))	Adapted from Fuenzalida and Ruegg (2019) quarter weekly SCC we assumed a healthy SCC of 50,000 SCC/ml in the other quarters and assuming equal MY for all quarters and averaging the SCC for all quarters
SCC at the mid point of a Gram-negative IMI episode	Triangular(a = ln(300), b = ln(800), c= ln(500))	Adapted from Fuenzalida and Ruegg (2019) quarter weekly SCC we assumed a healthy SCC of 50,000 SCC/ml in the other quarters and assuming equal MY for all quarters and averaging the SCC for all quarters
SCC at the end point of a Gram-negative IMI episode	Triangular(a = ln(50), b = ln(150), c= ln(100))	Adapted from Fuenzalida and Ruegg (2019) quarter weekly SCC we assumed a healthy SCC of 50,000 SCC/ml in the other quarters and assuming equal MY for all quarters and averaging the SCC for all quarters and (Bonestroo et al., 2021)
SCC at the beginning of a *Strep.* spp. IMI episode	Triangular(a = ln(160), b = ln(430), c= ln(300))	Adapted from Dalen et al. (2019a) where the minimum and maximum are based on the 95 % confidence interval
SCC at the mid point of a *Strep.* spp. IMI episode	Triangular(a = ln(100), b = ln(200), c= ln(150))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC at the end point of a *Strep.* spp. IMI episode	Triangular(a = ln(50), b = ln(150), c= ln(100))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC at the beginning of a NAS IMI episode	Triangular(a = ln(50), b = ln(350), c= ln(170))	Adapted from Dalen et al. (2019a) where the minimum and maximum are based on the 95 % confidence interval calculated using a weighted standard deviation of the NAS IMIs
SCC at the mid point of a NAS IMI episode	Triangular(a = ln(50), b = ln(200), c= ln(150))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC at the end point of a NAS IMI episode	Triangular(a = ln(50), b = ln(150), c= ln(100))	Adapted from Dalen et al. (2019a) and the general pattern in Bonestroo et al. (2021)
SCC non-recovery constant of *Staph. aureus* IMI episode	Ln(355)	Adapted from the reported mean inDalen et al. (2019a)
SCC non-recovery constant of Gram-negative IMI episode	Ln(2000)	Adapted from Fuenzalida and Ruegg (2019a) quarter weekly SCC we assumed a healthy SCC of 50,000 SCC/ml in the other quarters and assuming equal MY for all quarters and averaging the SCC for all quarters
SCC non-recovery constant of *Strep.* spp. IMI episode	Ln(300)	Adapted from the reported mean in Dalen et al. (2019a)
SCC non-recovery constant of NAS IMI episode	Ln(170)	Adapted from the reported mean in Dalen et al. (2019a) where a weighted mean was taken of all NAS IMIs
SCC healthy (IMI free)	Function dependent on DIM	–
Day-to-day variation SCC	Normal(0,0.80)	Based on SCC data from Bonestroo et al. (2022)
Milk yield	Based on a GAM model[1]	Bonestroo et al. (2022)
Clinical mastitis detected given clinical mastitis	Bernoulli(probability = 0.40)	Author's expertise
Clinical mastitis detected given no clinical mastitis	Bernoulli(probability = 1–0.99)	ISO (2007)
Dry cow treatment recovery *Staph. aureus*	Bernoulli(probability = 0.77)	Halasa et al. (2009b)
Dry cow treatment recovery Gram negative	Bernoulli(probability = 0.90)	Halasa et al. (2010)
Dry cow treatment recovery *Strep*. spp.	Bernoulli(probability = 0.89)	Halasa et al. (2009b)
Dry cow treatment recovery NAS	Bernoulli(probability = 0.81)	Newton et al. (2008)
Untreated dry cow period recovery *Staph. aureus*	Bernoulli(probability = 0.44)	Halasa et al. (2009b)
Untreated dry cow period recovery Gram negative	Bernoulli(probability = 0.60)	Huijps and Hogeveen (2007)
Untreated dry cow period recovery *Strep.* spp.	Bernoulli(probability = 0.47)	Halasa et al. (2009b)
Untreated dry cow period recovery NAS	Bernoulli(probability = 0.76)	Minor pathogens for untreated low SCC group in Swinkels et al. (2021)
Replacement period where cow spot was empty after culling	Poisson(lamba = 15)	Author's expertise
Labor farmer clinical mastitis check cow	0.10 h per activity	Author's expertise
Labor lactational treating cow	0.50 h per activity	Author's expertise
Labor dry cow treatment cow	0.50 h per activity	Author's expertise
Expected number of extra transmissions per infection day (transmission parameter beta) for *Staph. aureus*	0.00575 new infections per infected day	Average of Dalen et al. (2019b) and Skarbye et al. (2021)
Expected number of extra transmissions per infection day (transmission parameter beta) for Gram negative	0.0001 new infections per infected day	Gussmann et al. (2018)
Expected number of extra transmissions per infection day (transmission parameter beta) for *Strep.* spp.	0.003 new infections per infected day	Dalen et al. (2019b)
Expected number of extra transmissions per infection day (transmission parameter beta) for NAS	0.0048 new infections per infected day	Dalen et al. (2019b)

[1] A Generalized Additive Model (GAM) that models the association of SCC and DIM with milk yield using a non-linear function.

Table A2
The economic prices in the simulation model with their value and their sources.

Economic price	Value	Source
Milk price	€ 0.36 per kg	Blanken et al. (2019)
Feed cost correction milk price	€ 0.09 per kg	Adapted from Blanken et al. (2019)
Labor wage	€ 15.40 per hour	Adapted from Blanken et al. (2019)
Laboratory diagnostic price	€ 10.00 per test	Authors' expertise
Laboratory diagnostic use proportion	15 %	Adapted from Griffioen et al. (2016)
Involvement veterinarian in treatment	5 %	Lam et al. (2013)
Dry cow treatment costs	€ 11.00 per treatment	Scherpenzeel et al. (2018)
Lactational treatment	€ 35.00 per treatment	Lam et al. (2013)
Veterinarian price	€ 128.40 per hour	GD (2019)
Culling costs based on the slaughter value of the culled cow (revenue) and the opportunity costs of the replacement heifer (costs)	€ 297.00 per first-parity cow, € 212.00 per second-parity cow, € 186.00 per third-or-more-parity cow	Steeneveld et al. (2020)

et al., 2018; Halasa et al., 2009b). Culling was also an important cost factor, which was in line with previous research (Aghamohammadi et al., 2018; Halasa et al., 2009b; Huijps et al., 2008). Milk production losses were also an important cost factor. Nevertheless, the cost estimates of milk yield losses found in our study were lower than reported by van Soest et al. (2016), Huijps et al. (2008), and Aghamohammadi et al. (2018). This difference can be explained by the different methods of calculating subclinical mastitis milk production losses or the method of measuring SCC. We used a GAM model that found a nonlinear association between SCC and milk yield that is difficult to estimate with a linear model (Bonestroo et al., 2022). This GAM model estimated limited subclinical milk losses until 277,000 SCC/ml. As such, previous studies may have overestimated subclinical milk production losses at lower levels of SCC. To further investigate this, we have fitted a linear mixed model with SCC and SCC squared terms together with a random cow effect explaining milk yield and used it in the simulation model instead of a GAM model (data not shown). In that case, the subclinical milk production losses were similar to those reported in Aghamohammadi et al. (2018). Therefore, it is likely that the estimated non-linearity of the GAM model provided lower estimations of subclinical milk production losses at lower levels of SCC. This limited milk loss due to the non-linearity of the association may be due to the usage of on-farm SCC sensor data in the original study to estimate the association between SCC and milk yield. Further research on the association between SCC and milk yield using GAMs using laboratory SCC is needed to confirm this result.

In the model, we used a limited IMI pathogen population of 4 pathogen classes and assumed that a cow could only have one specific IMI ongoing at the time. This simplification was made due to the limited information available on other pathogens and the effects of having multiple pathogens at once on SCC and milk production. For the limited pathogen population, similar approaches were taken by others in the past (Halasa et al., 2009b; Østergaard et al., 2005). Nevertheless, the model could be adapted to add more pathogens to the pathogen population of the herd or the possibility to have multiple IMIs at once.

We used a large set of input variables to estimate the costs of chronic mastitis. Although we have tried to get a consistent set of input parameters, these input parameters were from multiple trials with multiple herds under various production circumstances. This variety of the sources increased the uncertainty of the parameters in the current model. The model was calibrated to model an average Dutch herd. However, farm and regional differences will still exist on individual farms, and therefore differences in the costs of mastitis will also exist between farms. Fortunately, the current model can be adapted to account for regional and price differences in the future. The availability of farm-specific sensor data opens up the opportunity to estimate farm-specific parameters (e.g., SCC parameters) or be used to approximate other herd-specific parameters (e.g., cure rate or transmission rate (Dalen et al., 2019a)). Sensor data can be used as a valuable addition in parameter estimation. It can increase the usefulness of these bio-economic models as decision-making tools for farmers in practice as the advice resulting from the model will be more pertained to the local farm reality. Nevertheless, the estimation of parameters in bioeconomic models remains to be heavily constrained by the availability of information from literature or experts. We simplified farmer behavior in the model to (sensor-based) decision rules and tied it to an action (e.g., antibiotic treatment or culling). In practice, farmer decision-making is complex. For instance, modeling the culling behavior of farmers is difficult as there are many reasons for culling cows. Bascom and Young (1998) indicated that mastitis is the primary reason in 15 % for the culling, but in 5 % and 2 % of culled cows as secondary or tertiary reasons. Therefore, it was difficult to model culling decisions in detail and likewise for the other decisions (e.g., when to apply antibiotic treatment). However, we would argue that this simplified approach is valuable. It allows the model user to estimate the cost of mastitis and chronic mastitis for different (sensor-based) decision rules relatively swiftly. Different sensor-based strategies can be operationalized relatively simply. These simple strategies can be focused on specific changes in procedures in this manner. As such, these simplified decision rules could be used to form economics-based and sensor-based farm procedures by experimenting with these rules in a simulation model before applying them in practice.

We decided to simplify transmission in the simulation model due to the uncertainty of transmission of contagious bacteria in AMS systems. The simplification of transmission may be considered as less realistic to transmission estimated using a susceptible-infected-recovered framework. More specifically, transmission is not as dynamic in our model as it assumes the same transmission rate, duration and case costs for the cases occurring due to transmission as the non-transmission cases. The transmission was calculated after each model iteration of the simulation model instead of using a susceptible-infected-recovered framework, as

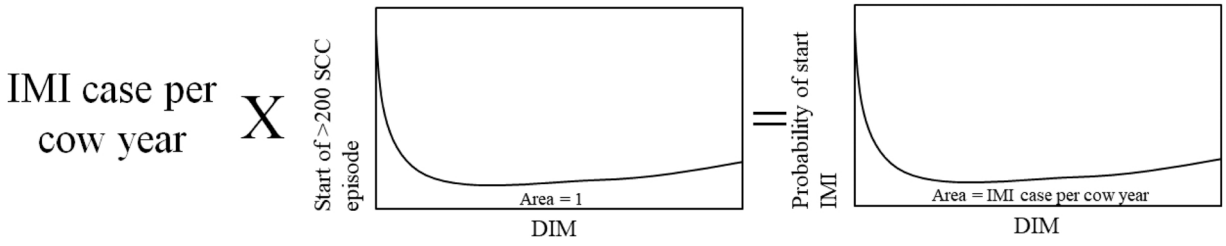


Fig. A1. The process of acquiring the incidence rate distribution of intramammary infections (IMI) based on the predefined IMI incidence rate parameter to indicate the level of IMI on a herd-level.

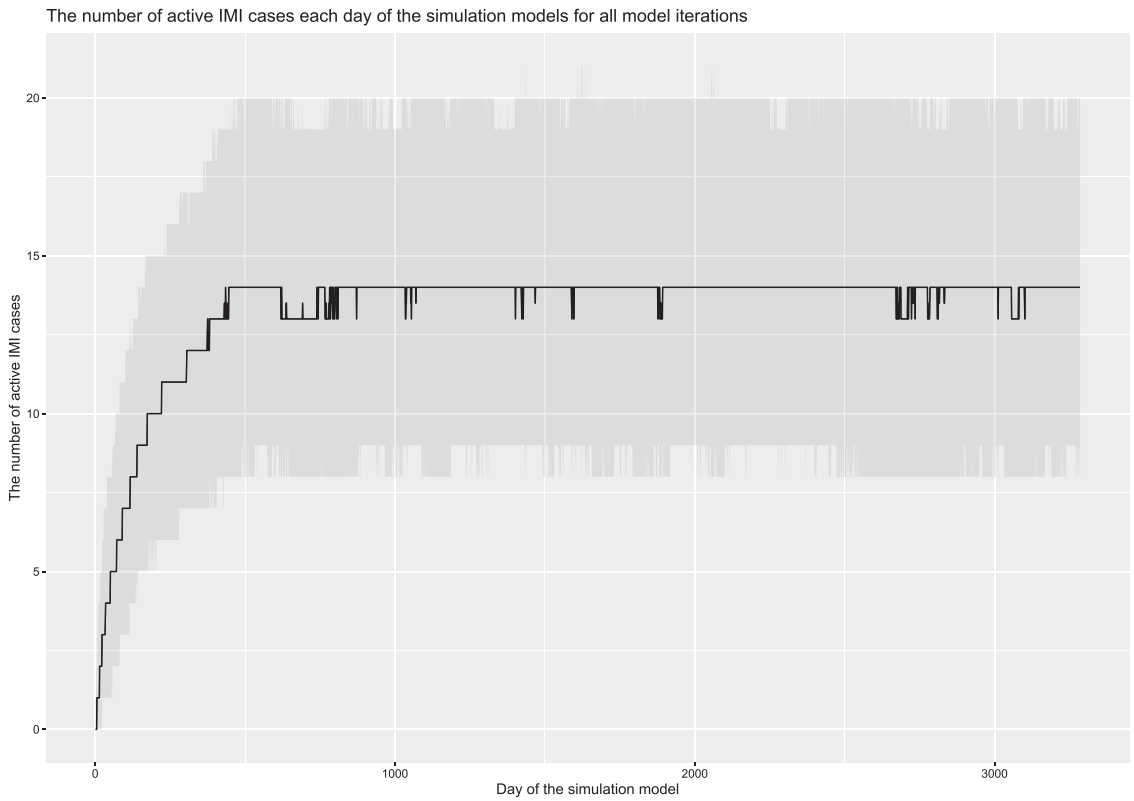


Fig. A2. The median (black line) and the 95 % quantile interval (shaded area) of the number of active cases (y-axis) over the number of simulated days in the simulation model.

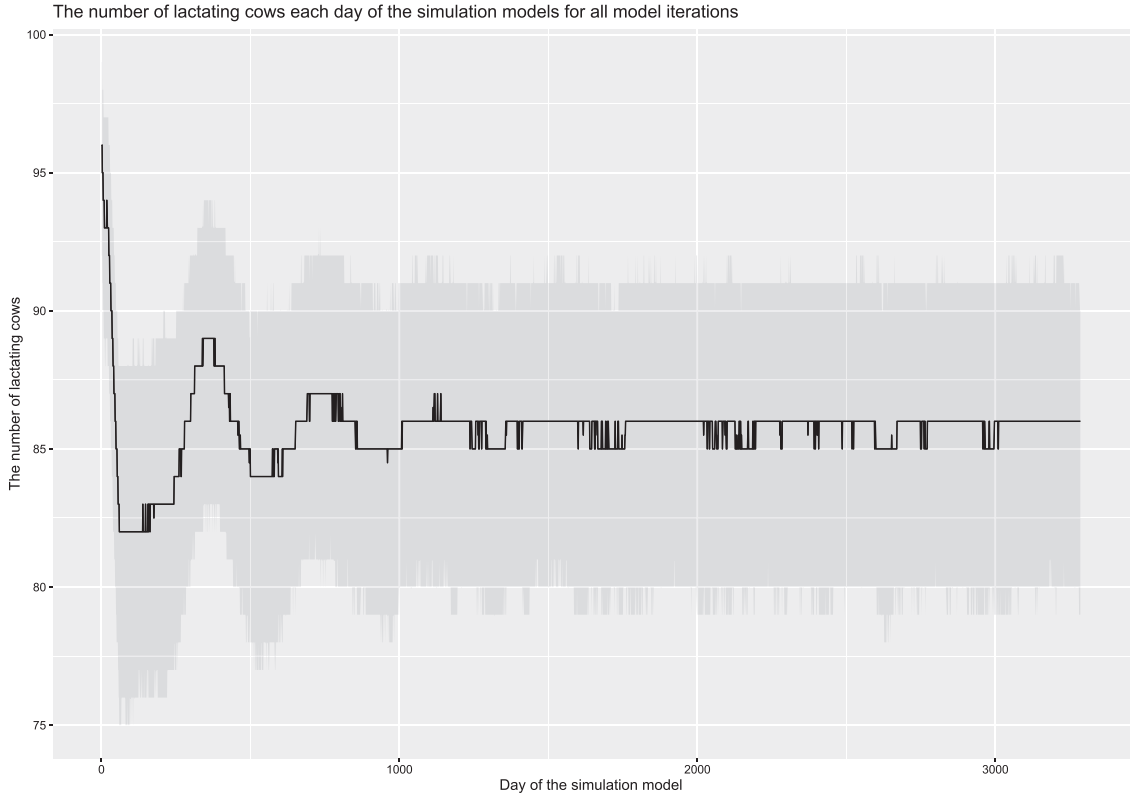


Fig. A3. The median (black line) and the 95 % quantile interval (shaded area) of the number of lactating cows (y-axis) over the number of simulated days in the simulation model.

done by Halasa et al. (2009a). The costs of transmission cases were estimated by multiplying the expected transmission cases with the pathogen-specific average costs of a mastitis case. Limited data were available on the transmission of several IMIs on a farm with AMS, making the estimation of transmission uncertain. It is somewhat likely that transmission modes on AMS farms are different from the transmission rates on conventional farms due to automated cleaning and disinfection procedures in milking robots. Currently, only Dalen et al. (2019a), Skarbye et al. (2021), and Deng et al. (2021) have recently reported transmission rates with current robots. It was only studied on either 1 or 2 farms for 4–17 months and for a limited number of pathogens. Other studies that measure transmission on AMS systems were unknown to the authors. We used the results of Dalen et al. (2019a) and Skarbye et al. (2021) as they covered the most pathogens. The differences in these studies indicate that the transmission rates vary substantially between farms and have a large confidence interval. Due to this uncertainty and variety, we wanted to separate the economic effect of contagious transmission to directly observe the effect of transmission. This could not be done using a susceptible-infected-recovered framework. The model would still return adequate estimates for the rest of the cost factors for non-transmission cases (e.g., milk yield losses), even if the transmission rate was wrongly specified, while a susceptible-infected-recovered framework would lead to a misleading result. Nevertheless, the considerable influence of transmission on the cost of mastitis can be seen in the results, and is in line with findings of other studies (Down et al., 2013; Halasa et al., 2009b). Our results confirm that extra costs due to transmission are a substantial factor in the total costs of mastitis and chronic mastitis.

We chose to use an adapted definition of mastitis chronicity during modeling based on Bonestroo et al. (2021). An IMI case was deemed chronic if it lasted longer than 4 weeks in IMI and elevated SCC. A definition with a longer minimum duration would lower chronic mastitis costs. However, Bonestroo et al. (2021) supply the only daily-SCC measurement-based chronic mastitis duration threshold, to our knowledge. Therefore, it was used for the adapted definition of mastitis chronicity in this study.

This study highlights the economic importance of chronic mastitis in the total costs of mastitis. Failure to completely recover early in the IMI episode was responsible for a substantial portion of the total costs of mastitis. The costs of chronic cases are more focused on the failure costs: the failure of a cure with and without treatment. Efforts have been made to assess the efficiency and effectiveness of treating chronic mastitis (St. Rose et al., 2003; Steeneveld et al., 2007; Swinkels et al., 2005a; b) for specific IMIs. Nevertheless, clinical mastitis has traditionally been focused on lactational treatment (Pyörälä, 2009). We estimated that 45 % of the costs of chronic mastitis are due to the transmission of contagious bacteria. Therefore, one of the most effective strategies to decrease the costs of chronic mastitis would be finding chronic cows and isolating them or improving milking procedures to reduce the risk of transmission during milking. Knowing the importance of chronic cases' costs helps us understand the potential benefits of better chronic mastitis prevention and management. Even though little research is performed on chronic mastitis detection, it shows the potential value of such models. With the current sensor technology, it may be possible to identify cows with chronic IMI episodes and possibly even predict cows that are expected to become chronic, allowing for identification and resulting interventions at an earlier stage.

5. Conclusion

Our results show that the median costs of chronic mastitis were € 118 and that the median total costs of mastitis were € 230. The share of the costs of chronic mastitis relative to the total mastitis costs was 51 %, this highlights the importance of chronic mastitis in the total costs of mastitis. The underlying causes of the costs of chronic mastitis were mainly the transmission of IMIs of ongoing cases, culling, and milk production losses. In terms of pathogen impact, *Staph. aureus* caused the largest share of the costs of chronic mastitis. As current developments in the application of sensors enable better identification of chronic mastitis, prevention and management of chronic mastitis should get more attention in the future.

Potential conflicts of interests

John Bonestroo and Ilka C. Klaas are employed by DeLaval International AB. Mariska van der Voort, Nils Fall, Ulf Emanuelson, and Henk Hogeveen have no conflict of interest to report.

Acknowledgments and funding

This research was funded by an Industry Ph.D.-program of the Swedish Government, reference number N2017/036895/SK, and DeLaval International AB (Tumba, Sweden).

Appendix A. The model parameters with references

See Tables A1 and A2.

Appendix B. The estimation of the probability of obtaining IMI

We used SCC data as a proxy to estimate the distribution of IMI throughout the cow lactation. A logistic Generalized Additive Model (GAM) was fitted that predicted whether the SCC was higher than 200,000 for the first time during an episode (dependent variable) based on DIM (independent variable). The start of the episode was determined by checking whether the mean SCC of the next 25 days was higher than 200,000 SCC/ml. As we did not have access to the probability of being infected for every DIM, we have used the SCC-based GAM to obtain a proxy for these probabilities based on increased SCC, see Fig. 1. A probability was predicted for each DIM between 1 and 305. These probabilities were normalized to be summed up to 1 (the area under the curve in Fig. 1). This probability of increased SCC was used as a proxy for a probability of IMI. The probability of IMI for each DIM was calculated by multiplying these normalized values with the incidence rates of IMI for primiparous and multiparous cows. For DIM after 305. i.e., for longer lactations, the probability of infection was assumed to be equal to the probability of infection at 305 DIM. For each time step and IMI-free cow, the probability of an IMI was retrieved from these "curves." (Fig. A1).

For each time step and each that cow did not have an IMI, the probability of an IMI was retrieved from these "curves."

Appendix C. The convergence of the number of IMI cases and number of lactations

(Figs. A2 and A3).

References

Aghamohammadi, M., Haine, D., Kelton, D.F., Barkema, H.W., Hogeveen, H., Keefe, G.P., Dufour, S., 2018. Herd-level mastitis-associated costs on Canadian dairy farms. Front. Vet. Sci. 5, 100.

ISO, 2007. ISO/DIS 20966: Automatic milking installations—Requirements and testing. Geneva.

International Dairy Federation, 2011. Suggested Interpretation of Mastitis Terminology (revision of Bulletin of IDF N° 338/1999). Brussels.

KNMvD, 2018. Richtlijn droogzetten melkkoeien [WWW Document]. URL ⟨https://www.knmvd.nl/app/uploads/2018/07/RICHTLIJN-DROOGZETTEN-MELKKOEIEN.pdf⟩ (accessed 6.15.21).

GD, 2019. Producten en tarieven [WWW Document]. URL ⟨https://www.gddiergezondheid.nl/~/media/Files/DAPContact/Productenentarieven2019⟩.as (accessed 1.28.22).

Bar, D., Gröhn, Y.T., Bennett, G., Gonzalez, R.N., Hertl, J.A., Schulte, H.F., Tauer, L.W., Welcome, F.L., Schukken, Y.H., 2007. Effect of repeated episodes of generic clinical mastitis on milk yield in dairy cows. J. Dairy Sci. 90, 4643–4653.

Bascom, S.S., Young, A.J., 1998. A summary of the reasons why farmers cull cows. J. Dairy Sci. 81, 2299–2305.

Berends, I., Swart, W., Frankena, K., Muskens, J., Lam, T., Van Schaik, G., 2008. The effect of becoming BVDV-free on fertility and udder health in Dutch dairy herds. Prev. Vet. Med. 84, 48–60.
Blanken, K., de Buisonje, F., Evers, A., Ouweltjes, W., Verkaik, J., Vermeij, I., Wemmenhove, H., 2019. KWIN 2019–2020: Kwantitatieve Informatie Veehouderij. Wageningen Livestock Research.
Bonestroo, J., van der Voort, M., Fall, N., Hogeveen, H., Emanuelson, U., Klaas, I.C., 2021. Progression of different udder inflammation indicators and their episode length after onset of inflammation using automatic milking system sensor data. J. Dairy Sci. 104, 3457–3473.
Bonestroo, J., van der Voort, M., Fall, N., Emanuelson, U., Klaas, I.C., Hogeveen, H., 2022. Estimating the nonlinear association of online somatic cell count, lactate dehydrogenase, and electrical conductivity with milk yield. J. Dairy Sci. 105 (4), 3518–3529.
Dalen, G., Rachah, A., Nørstebø, H., Schukken, Y.H., Reksen, O., 2019a. Dynamics of somatic cell count patterns as a proxy for transmission of mastitis pathogens. J. Dairy Sci. 102, 11349–11358.
Dalen, G., Rachah, A., Nørstebø, H., Schukken, Y.H., Reksen, O., 2019b. The detection of intramammary infections using online somatic cell counts. J. Dairy Sci. 102, 5419–5429.
De Serres, G., Gay, N.J., Farrington, C.P., 2000. Epidemiology of transmissible diseases after elimination. Am. J. Epidemiol. 151, 1039–1048.
Deng, Z., Koop, G., Hogeveen, H., Fischer, E.A.J., van den Borne, B.H.P., van der Tol, R., Lam, T.J.G.M., 2021. Transmission dynamics of Staphylococcus aureus and Streptococcus agalactiae in a Dutch dairy herd using an automatic milking system. Prev. Vet. Med. 192, 105384.
Dijkhuizen, A.A., Morris, R.S., 1997. Animal health economics. Princ. Appl. Univ. Sidney, Sidney.
Down, P.M., Green, M.J., Hudson, C.D., 2013. Rate of transmission: a major determinant of the cost of clinical mastitis. J. Dairy Sci. 96, 6301–6314.
Fuenzalida, M.J., Ruegg, P.L., 2019. Negatively controlled, randomized clinical trial to evaluate intramammary treatment of nonsevere, gram-negative clinical mastitis. J. Dairy Sci. 102, 5438–5457.
Griffioen, K., Hop, G.E., Holstege, M.M.C., Velthuis, A.G.J., Lam, T.J.G.M., Consortium, 1Health4Food–Dutch Mastitis Diagnostics, 2016. Dutch dairy farmers' need for microbiological mastitis diagnostics. J. Dairy Sci. 99, 5551–5561.
Gussmann, M., Kirkeby, C., Græsbøll, K., Farre, M., Halasa, T., 2018. A strain-, cow-, and herd-specific bio-economic simulation model of intramammary infections in dairy cattle herds. J. Theor. Biol. 449, 83–93.
Hadrich, J.C., Wolf, C.A., Lombard, J., Dolak, T.M., 2018. Estimating milk yield and value losses from increased somatic cell count on US dairy farms. J. Dairy Sci. 101, 3588–3596.
Halasa, T., Nielen, M., Whist, A.C., Østerås, O., 2009a. Meta-analysis of dry cow management for dairy cattle. Part 2. Cure of existing intramammary infections. J. Dairy Sci. 92, 3150–3157.
Halasa, T., Nielen, M., van, Huirne, R.B.M., Hogeveen, H., 2009b. Stochastic bio-economic model of bovine intramammary infection. Livest. Sci. 124, 295–305.
Halasa, T., Østerås, O., Hogeveen, H., van Werven, T., Nielen, M., 2009c. Meta-analysis of dry cow management for dairy cattle. Part 1. Protection against new intramammary infections. J. Dairy Sci. 92, 3134–3149.
Halasa, T., Nielen, M., van Werven, T., Hogeveen, H., 2010. A simulation model to calculate costs and benefits of dry period interventions in dairy cattle. Livest. Sci. 129, 80–87.
Hogan, J., Smith, K.L., 2003. Coliform mastitis. Vet. Res. 34, 507–519.
Hogeveen, H., Kamphuis, C., Steeneveld, W., Mollenhorst, H., 2010. Sensors and clinical mastitis—The quest for the perfect alert. Sensors 10, 7991–8009.
Hogeveen, H., Steeneveld, W., Wolf, C.A., 2019. Production diseases reduce the efficiency of dairy production: a review of the results, methods, and approaches regarding the economics of mastitis. Annu. Rev. Resour. Econ. 11, 289–312.
Hortet, P., Seegers, H., 1998. Loss in milk yield and related composition changes resulting from clinical mastitis in dairy cows. Prev. Vet. Med. 37, 1–20.
Huijps, K., Hogeveen, H., 2007. Stochastic modeling to determine the economic effects of blanket, selective, and no dry cow therapy. J. Dairy Sci. 90, 1225–1234.
Huijps, K., Lam, T.J.G.M., Hogeveen, H., 2008. Costs of mastitis: facts and perception. J. Dairy Res. 75, 113–120.
Lam, T., Van Den Borne, B.H.P., Jansen, J., Huijps, K., Van Veersen, J.C.L., Van Schaik, G., Hogeveen, H., 2013. Improving bovine udder health: a national mastitis control program in the Netherlands. J. Dairy Sci. 96, 1301–1311.
Nash, D.L., Rogers, G.W., Cooper, J.B., Hargrove, G.L., Keown, J.F., 2002. Relationships among severity and duration of clinical mastitis and sire transmitting abilities for somatic cell score, udder type traits, productive life, and protein yield. J. Dairy Sci. 85, 1273–1284.
Newton, H.T., Green, M.J., Benchaoui, H., Cracknell, V., Rowan, T., Bradley, A.J., 2008. Comparison of the efficacy of cloxacillin alone and cloxacillin combined with an internal teat sealant for dry-cow therapy. Vet. Rec. 162, 678–683.
Nor, N.M., Steeneveld, W., Hogeveen, H., 2014. The average culling rate of Dutch dairy herds over the years 2007 to 2010 and its association with herd reproduction, performance and health. J. Dairy Res. 81, 1–8.
Nørstebø, H., Dalen, G., Rachah, A., Heringstad, B., Whist, A.C., Nødtvedt, A., Reksen, O., 2019. Factors associated with milking-to-milking variability in somatic cell counts from healthy cows in an automatic milking system. Prev. Vet. Med. 172, 104786.
Oliveira, L., Hulland, C., Ruegg, P.L., 2013. Characterization of clinical mastitis occurring in cows on 50 large dairy herds in Wisconsin. J. Dairy Sci. 96, 7538–7549.
Østergaard, S., Chagunda, M.G.G., Friggens, N.C., Bennedsgaard, T.W., Klaas, I.C., 2005. A stochastic model simulating pathogen-specific mastitis control in a dairy herd. J. Dairy Sci. 88, 4243–4257.
Pyörälä, S., 2009. Treatment of mastitis during lactation. Ir. Vet. J. 62, S40.
Santman-Berends, I., Lam, T., Keurentjes, J., Van Schaik, G., 2015. An estimation of the clinical mastitis incidence per 100 cows per year based on routinely collected herd data. J. Dairy Sci. 98, 6965–6977.
Sargent, R.G., 2010. Verification and validation of simulation models, in: Proceedings of the 2010 Winter Simulation Conference. IEEE, pp. 166–183.
Scherpenzeel, C.G.M., Hogeveen, H., Maas, L., Lam, T., 2018. Economic optimization of selective dry cow treatment. J. Dairy Sci. 101, 1530–1539.
Seegers, H., Fourichon, C., Beaudeau, F., 2003. Production effects related to mastitis and mastitis economics in dairy cattle herds. Vet. Res. 34, 475–491.
Skarbye, A.P., Krogh, M.A., Denwood, M., Bjerring, M., Østergaard, S., 2021. Effect of enhanced hygiene on transmission of Staphylococcus aureus, Streptococcus agalactiae, and Streptococcus dysgalactiae in dairy herds with automatic milking systems. J. Dairy Sci. 104, 7195–7209.
van Soest, F.J.S., Santman-Berends, I.M.G.A., Lam, T.J.G.M., Hogeveen, H., 2016. Failure and preventive costs of mastitis on Dutch dairy farms. J. Dairy Sci. 99, 8365–8374.
Sol, J., Sampimon, O.C., Barkema, H.W., Schukken, Y.H., 2000. Factors associated with cure after therapy of clinical mastitis caused by Staphylococcus aureus. J. Dairy Sci. 83, 278–284.
St. Rose, S.G.S., Swinkels, J.M., Kremer, W.D.J., Kruitwagen, C.L.J.J., Zadoks, R.N., 2003. Effect of penethamate hydriodide treatment on bacteriological cure, somatic cell count and milk production of cows and quarters with chronic subclinical Streptococcus uberis or Streptococcus dysgalactiae infection. J. Dairy Res. 70, 387–394.
Steeneveld, W., Swinkels, J., Hogeveen, H., 2007. Stochastic modelling to assess economic effects of treatment of chronic subclinical mastitis caused by Streptococcus uberis. J. Dairy Res. 74, 459–467.
Steeneveld, W., Amuta, P., van Soest, F.J.S., Jorritsma, R., Hogeveen, H., 2020. Estimating the combined costs of clinical and subclinical ketosis in dairy cows. PLoS One 15, e0230448.
Swinkels, J., Hogeveen, H., Zadoks, R.N., 2005a. A partial budget model to estimate economic benefits of lactational treatment of subclinical Staphylococcus aureus mastitis. J. Dairy Sci. 88, 4273–4287.
Swinkels, J.M., Leach, K.A., Breen, J.E., Payne, B., White, V., Green, M.J., Bradley, A.J., 2021. Randomized controlled field trial comparing quarter and cow level selective dry cow treatment using the California Mastitis Test. J. Dairy Sci. 104, 9063–9081.
Swinkels, Rooijendijk, J.G.A., Zadoks, R.N., Hogeveen, H., 2005b. Use of partial budgeting to determine the economic benefits of antibiotic treatment of chronic subclinical mastitis caused by Streptococcus uberis or Streptococcus dysgalactiae. J. Dairy Res. 72, 75–85.
Taponen, S., Simojoki, H., Haveri, M., Larsen, H.D., Pyörälä, S., 2006. Clinical characteristics and persistence of bovine mastitis caused by different species of coagulase-negative staphylococci identified with API or AFLP. Vet. Microbiol. 115, 199–207.
Taponen, S., Liski, E., Heikkilä, A.-M., Pyörälä, S., 2017. Factors associated with intramammary infection in dairy cows caused by coagulase-negative staphylococci, Staphylococcus aureus, Streptococcus uberis, Streptococcus dysgalactiae, Corynebacterium bovis, or Escherichia coli. J. Dairy Sci. 100, 493–503.
Todhunter, D.A., Cantwell, L.L., Smith, K.L., Hoblet, K.H., Hogan, J.S., 1993. Characteristics of coagulase-negative staphylococci isolated from bovine intramammary infections. Vet. Microbiol. 34, 373–380.
Valckenier, D., Piepers, S., Schukken, Y.H., De Visscher, A., Boyen, F., Haesebrouck, F., De Vliegher, S., 2021. Longitudinal study on the effects of intramammary infection with non-aureus staphylococci on udder health and milk production in dairy heifers. J. Dairy Sci. 104, 899–914.
Van den Borne, B.H.P., Van Schaik, G., Lam, T.J.G.M., Nielen, M., 2010. Therapeutic effects of antimicrobial treatment during lactation of recently acquired bovine subclinical mastitis: Two linked randomized field trials. J. Dairy Sci. 93, 218–233.
Wente, N., Grieger, A.S., Klocke, D., Paduch, J.-H., Zhang, Y., Leimbach, S., Tho Seeth, M., Mansion-De Vries, E.M., Mohr, E., Krömker, V., 2020. Recurrent mastitis–persistent or new infections? Vet. Microbiol. 244, 108682.
Wilson, D.J., Gonzalez, R.N., Case, K.L., Garrison, L.L., Gröhn, Y.T., 1999. Comparison of seven antibiotic treatments with no treatment for bacteriological efficacy against bovine mastitis pathogens. J. Dairy Sci. 82, 1664–1670.
Zadoks, R.N., Gillespie, B.E., Barkema, H.W., Sampimon, O.C., Oliver, S.P., Schukken, Y. H., 2003. Clinical, epidemiological and molecular characteristics of Streptococcus uberis infections in dairy herds. Epidemiol. Infect. 130, 335–349.